Neocortical excitation/inhibition balance in information processing and social dysfunction.

Journal: Nature

Publication Year: 2011

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PubMed link: 21796121

Funding Grants: Bioengineering technology for fast optical control of differentiation and function in stem cells and stem cell progeny

Public Summary:

Scientific Abstract:
Severe behavioural deficits in psychiatric diseases such as autism and schizophrenia have been hypothesized to arise from elevations in the cellular balance of excitation and inhibition (E/I balance) within neural microcircuitry. This hypothesis could unify diverse streams of pathophysiological and genetic evidence, but has not been susceptible to direct testing. Here we design and use several novel optogenetic tools to causally investigate the cellular E/I balance hypothesis in freely moving mammals, and explore the associated circuit physiology. Elevation, but not reduction, of cellular E/I balance within the mouse medial prefrontal cortex was found to elicit a profound impairment in cellular information processing, associated with specific behavioural impairments and increased high-frequency power in the 30-80 Hz range, which have both been observed in clinical conditions in humans. Consistent with the E/I balance hypothesis, compensatory elevation of inhibitory cell excitability partially rescued social deficits caused by E/I balance elevation. These results provide support for the elevated cellular E/I balance hypothesis of severe neuropsychiatric disease-related symptoms.